

**ASSESSMENT OF THE EFFECTS OF LOW DOSES OF MEIQX ON  
MEIQX-DNA ADDUCT FORMATION IN ANIMALS AND  
HUMANS.**

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2-Amino-3,4-dimethylimidazo[4,5-f]quinoxaline (MeIQx) is a heterocyclic amine that has been found in cooked foods, particularly meat. MeIQx is mutagenic in a number of test systems and carcinogenic in rats and mice. Human exposure to MeIQx via dietary sources has been estimated as low as a few ng/kg/day to levels as high as  $\approx 4 \mu\text{g/kg/day}$ . Most animal studies, however, have been conducted at doses in excess of 10 mg/kg/day. We have used a combination of accelerator mass spectrometry (AMS), <sup>32</sup>P-postlabeling and HPLC to study the dosimetry of MeIQx DNA adduct formation under both acute and chronic exposures in animals and compare these levels to the MeIQx adducts formed in human colon. <sup>14</sup>C-MeIQx was administered to Sprague-Dawley rats daily in the diet for 6 weeks at doses of 1 ng/kg/day - 34  $\mu\text{g/kg/day}$ . Additionally, 2 human volunteers were given <sup>14</sup>C-MeIQx (3  $\mu\text{g/kg}$ ) and the colon adduct levels were measured. The results of these studies show: 1) adducts accumulate in the tissues of the rat for 30 days before reaching steady-state under chronic exposure conditions. 2) MeIQx DNA adduct levels in rats decrease linearly with decreasing dose for single dose studies 3) adduct clearance in the rat may be dose dependent, 4)  $\geq 90\%$  of the MeIQx DNA adducts in both rodent and human colon is the dG-C8 adduct, and 5) the levels of adducts found in human colon, based on calculated covalent binding indices, are 13 times greater than the adduct levels found in rodent colons at an equivalent dose. These data suggest that while the same adducts are present in rodents and humans, human colon may be more sensitive to MeIQx than the rodent colon.

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